

Tacrolimus in membranous nephropathy

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To the Editor: In a recent issue of the Journal, Praga *et al.*¹ reported their experience with tacrolimus monotherapy in patients with idiopathic membranous nephropathy. The authors concluded that tacrolimus was a very useful therapeutic option. This conclusion was based on the findings of a higher remission rate and a reduced risk of deterioration of renal function in the treated patients.

However, some of the reported data need clarification.

- (1) This study may not be applicable to routine clinical practice. Most studies included patients with relatively recent onset of disease. In the study of Praga *et al.*, the interval between diagnosis and inclusion in the study was 45 months in the control group and 58 months in the treated group. Most patients with idiopathic membranous nephropathy will develop remission or renal failure within 3 years after presentation.²
- (2) The information on follow-up time is lacking. The study included patients studied between January 2003 and September 2006. It is therefore unlikely that all patients have been followed for 30 months. This information is needed to read Figure 3 correctly. The cumulative incidence of a relapse may be higher than shown.
- (3) The power calculation suggests that the study was powered to determine differences in remission rate and not differences in renal failure rate.

Moreover the results are overrated and so is the conclusion. Tacrolimus treatment did not result in persistent remissions, since the number of remissions at the end of follow-up was similar in the treated and the control groups. The shortlasting decrease of proteinuria may be the consequence of a hemodynamic effect. Correct interpretation of these results would be that 18 months of treatment with tacrolimus did not influence the outcome with respect to remissions at the end of follow-up. Certainly, the conclusion reached by the authors is driven by the observed differences in renal function deterioration. In the control group, six patients developed a 50% increase of serum creatinine level as compared to only one in the treated group. One normally would have expected that differences in renal survival become evident with longer duration of follow-up. However, Figure 5 shows that the differences between the groups were already apparent at 6 months after randomization, and that there was no further change in renal function after 12 months. Patients who reached the renal failure end point were characterized by higher age, higher initial serum creatinine concentration, and higher levels of proteinuria. Table 1 clearly indicates that the treated and the control groups were not balanced with respect

to these parameters. The control group contained more patients aged >50 years (48 vs 24%), more patients with glomerular filtration rate <60 ml min⁻¹ (17 vs 4%), and more patients with severe proteinuria (43 vs 32%). These differences must not be overlooked; the β error is high in a small-sized study.

Therefore, this study does not allow to conclude that tacrolimus improves renal survival in patients with idiopathic membranous nephropathy. Thus far, only alkylating agents have been proven effective in reducing the risk of end-stage renal disease.²⁻⁴

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Mortality effect of coronary calcification and phosphate binder choice in incident hemodialysis patients. No good evidence to promote a general use of sevelamer

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To the Editor: There is little doubt that coronary calcification is associated with cardiovascular mortality.

Also, plausible biologic explanations implying disturbed calcium phosphate metabolisms are available. A practicing nephrologist may therefore be tempted to switch from the traditional calcium-based chelators to other alternatives. One of those attractive alternatives is sevelamer, which has been shown to reduce coronary calcification.

However, coronary calcification is only a surrogate marker, and clinical trials with improvement of surrogate markers may not necessarily be associated with better clinical outcomes. Worse still, in some of them, just to cite the